Pharmacogenomics of antithrombotic drugs – a novel study design and data collection approach using Finnish biobanks and national registries

Anna-Leena Vuorinen[1], Jaakko Lähteenmäki[1], Mika Lehto[2], Kari Harno[3], Maija Wolf[4], Mikko Niemi[5]

[1] VTT Technical Research Centre of Finland Ltd, [2] Hospital District of Helsinki and Uusimaa,
[3] University of Eastern Finland, [4] Medaffcon Oy, [5] University of Helsinki

Background

Adverse drug reactions cause hospitalizations and even premature deaths. Pharmacogenetic studies have identified a number of gene variants that cause adverse drug responses in individuals using antithrombotic drugs. Certain gene variants affect drug metabolism increasing the risk for bleeding.

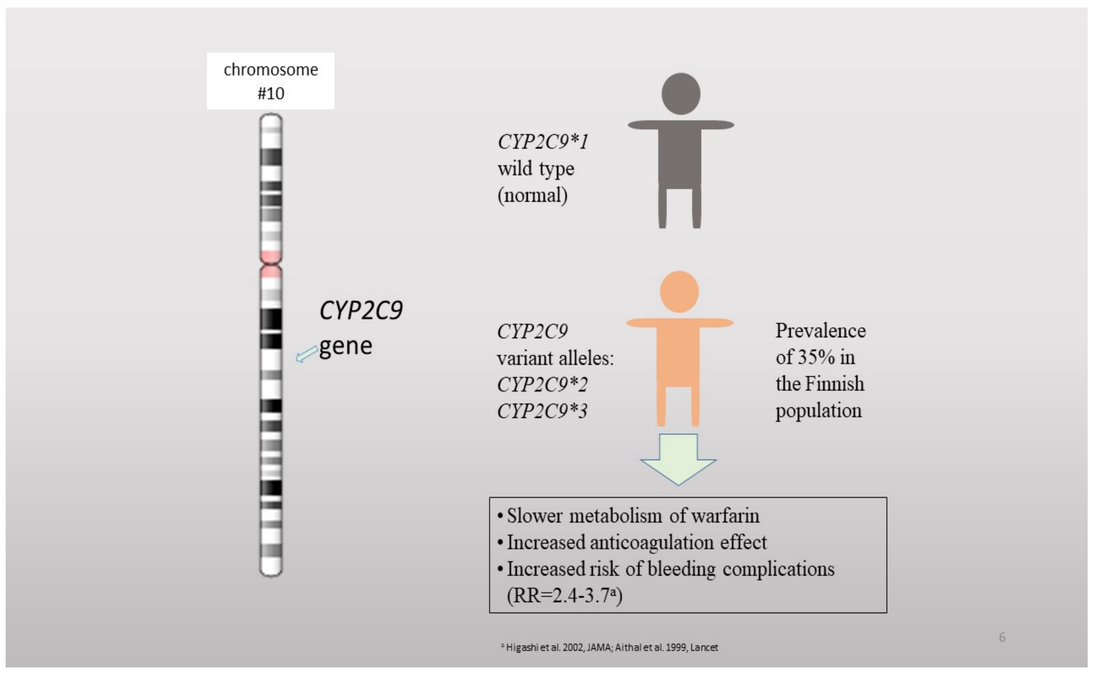

Figure 1. Prevalence of CYP2C9 variant alleles and their association with warfarin therapy.

Objectives

To investigate clinical and economic feasibility of using genomic data in the context of antithrombotic drug therapy by linking data from Finnish biobanks and national registries.

The specific objectives are:

1. To investigate clinical response to warfarin therapy in individuals with and without specific genetic variants
2. To assess the clinical and economic impact of using genotype data in guiding warfaring therapy
3. To employ data-driven classification methods to explore genotype-phenotype associations for antithrombotic drugs, including direct oral anticoagulants, clopidogrel and heparins

Data sources

The following data and data sources are intended to be used:

- Genotype data (Helsinki Biobank, THL Biobank, Auria Biobank)
- Laboratory data (laboratory registers)
- Healthcare encounters (National Institute for Health and Welfare)
- Drug purchases (Social Insurance Institution)
- Electronic health records

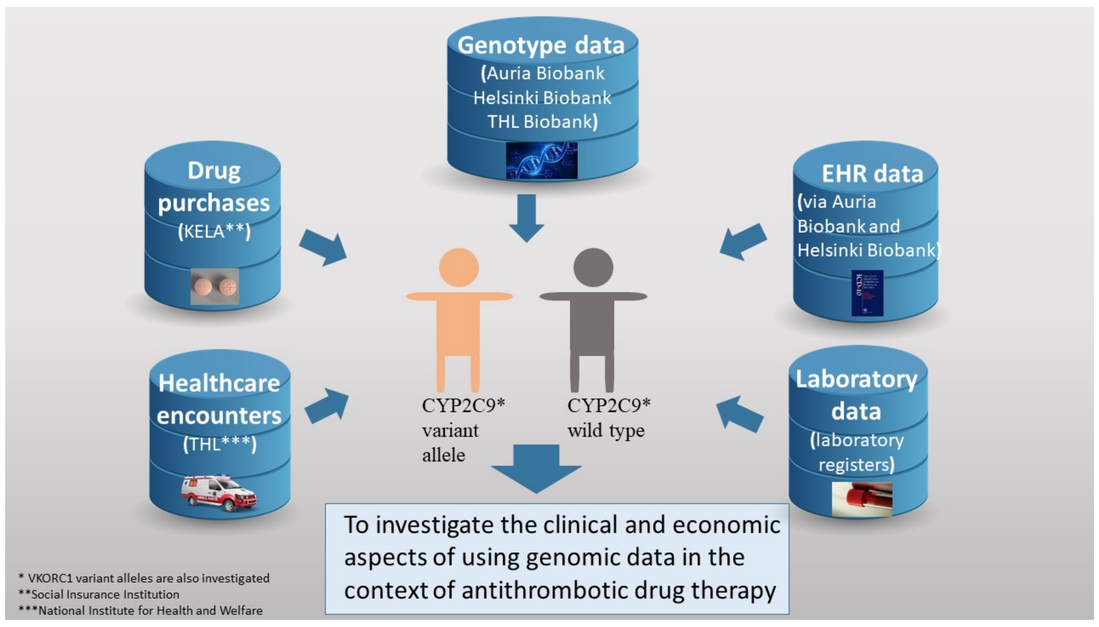

Figure 2. Data sources.

Participants

Inclusion criteria:

- ≥ 18 years of age
- Genotyped for variants in *CYP2C9* and *VKORC1*
- Diagnosed with a disease of cardiovascular system.
- Purchased at least one of the following antithrombotic drugs between 1.1.2007 - 31.12.2018:
  - Warfarin, Dabigatran, Rivaroxaban, Apixaban, Edoxaban, Heparin, Enoxaparin, Dalteparin, Clopidogrel, Ticagrelor, Acetylsalicylic acid

Sample size: 2678 patients are required to detect a risk ratio (RR) of 1.8 for bleeding complications in carriers of variant alleles *CYP2C9*2* and *CYP2C9*3* (α=0.05, power=0.9).

Outcomes measures

- Bleeding complications in warfarin users
- Time in Therapeutic Range (TTR) in warfarin users
- Drug dosage in warfarin users
- Healthcare encounters in warfarin users
- Clinical response to other antithrombotic drugs
- Interactions with other drugs

Status and next steps

- **Preparatory phase on-going (data permit applications and contracts)**
- **Data analysis planned to begin in September 2019 (FinnGen genome data to be released for biobank studies)**
- **The study is carried out in the framework of the PreMed project**

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PreMed project

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Contact
Anna-Leena Vuorinen
Tel. +358408485966
anna-leena.vuorinen@vtt.fi